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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/766,412	01/22/2001	Ruowen Ge	1781-0215P	7335

2292 7590 09/21/2005

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EXAMINER

MOHAMED, ABDEL A

ART UNIT PAPER NUMBER

1654

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/766,412

Applicant(s)

GE ET AL.

Examiner

Abdel A. Mohamed

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 July 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2, 6-8, 10, 13-16, 19, 20, 22, 23 and 25-32 is/are pending in the application.
- 4a) Of the above claim(s) 10, 15, 16, 20, 23, 25-28 and 30-32 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 6-8, 13, 14, 19, 22 and 29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

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DETAILED ACTION

ACKNOWLEDGMENT TO AMENDMENT, REMARKS, STATUS OF THE APPLICATION AND CLAIMS

1. The amendment and remarks filed 07/08/05 are acknowledged, entered and considered. In view of Applicant's request claims 10 and 25 have been amended and claims 30-32 have been added. Claims 1, 2, 6-8, 10, 13-16, 19, 20, 22, 23 and 25-32 are now pending in the application of which claims 10, 15, 16, 20, 23 and including 25-28 (i.e., because Applicant amended claim 25 to depend on non-elected claim 10) are withdrawn as non-elected invention for the reasons of record, and newly presented claims 30-32 are withdrawn for election by original presentation (See *infra*). Thus, the Office action is directed to the merits of claims 1, 2, 6-8, 13, 14, 19, 22 and 29 as *per* elected invention. The rejections under 35 U.S.C. 112, first paragraph for claim 22 and 35 U.S.C. 112, first paragraph for claims 1, 2, 6-8, 13, 14, 19, 22 and 29 are maintained for the reasons of record. However, the objection to the specification is withdrawn in view of Applicant's amendment filed 07/08/05. Claims 25-27 were objected and indicated as allowable subject matter if rewritten in independent form including all the limitations of base claims and any intervening claims in the previous Office action. Nevertheless, since Applicant has amended claim 25 to depend on non-elected claim 10, the indication of allowable subject matter is withdrawn because of the claims being dependent on non-elected invention.

ELECTION BY ORIGINAL PRESENTATION

2. Newly submitted claims 30-32 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claims 30-32 depend on non-elected SEQ ID NOS:29, 31 and 32, respectively. Applicant attention is directed to restriction requirement mailed on 08/25/03 as paper No. 8 which states that the sequences are patentably distinct because they are unrelated sequences and each unrelated sequences is considered a separate and distinct product.

Since Applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 30-32 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

ARGUMENTS ARE NOT PERSUASIVE

3. Applicant's arguments filed 07/08/05 have been considered but they are unpersuasive. In regard to **ELECTION OF SPECIES**, Applicant has argued that withdrawing claims 10, 15, 16, 20 and 23 from consideration is not justified because pending claims 1, 2, 6-8, 10, 13-16, 19, 20, 22, 23 and 25-29 all ***read or relate to the elected species*** is unpersuasive. Contrary to Applicant's arguments, the election/restriction was **not an election of species**, rather, it was a restriction requirement in which Applicant was required to elect a single sequence for examination, and Applicant was reminded that this was **a restriction requirement, not an election**

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of species (See e.g., page 4, last line of the first paragraph on the election/restriction requirement mailed on 08/25/03 as Paper No. 8). Further, in response to the requirement for election, Applicant elected SEQ ID NO:30 with traverse (See e.g., page 8, second paragraph of Applicant's response filed 09/25/03). Thus, the restriction requirement was not an election of species and Applicant never challenged it in the previous communications. Hence, claims 10, 15, 16, 23, 25-28 and 30-32 are withdrawn as non-elected inventions for the reasons of record.

REPLY TO FINAL MUST INCLUDE CANCELLATION

4. This application contains claims 10, 15, 16, 20, 23, 25-28 and 30-32 drawn to an invention nonelected with traverse in communication filed 09/25/03. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

CLAIMS REJECTION-35 U.S.C. 112, ^{1st} PARAGRAPH

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 22 remains rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to

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one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no description in the instant specification for the claimed method of **preventing or treating a subject** for the conditions being claimed, such as primary tumor growth or metastasis by inhibiting tumor angiogenesis.

Applicant has argued that typical of the claim in question is claim 23. The claim in question does not recite that tumors are being prevented (nor it recites that a subject is being prevented). Instead, the claim recites (in part) that the **growth or metastasis** of tumors that already exist in a subject ("a subject presenting a tumor) is treated or prevented. Thus, the invention in question involves (among other things) preventing tumor growth or metastasis. Further, Applicant argues that the specification describes the claimed invention and cites page 8, lines 6-11 for the effective doses of the peptides administered is unpersuasive. Contrary to Applicant's arguments, the typical of the claim in question is not claim 23 (claim 23 is withdrawn as non-elected invention); rather, the claim in question is claims 22. As argued by Applicant, the claim is not directed to inhibit and/or prevent the existing tumor from further growth. It is directed to prevent or treat primary tumor growth or metastasis.

Applicant's attention is directed to the definition of metastasis on page 945 of Dorland's Illustrated Medical Dictionary, Twenty-fifth Edition, published by W.B. Saunders, 1974 which defines **metastasis** as the transfer of diseases from one organ or part to another not directly connected with it. It may be due either to the transfer of pathogenic microorganisms (e.g., tubercle bacilli) or transfer of cell, as in malignant

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tumors. The capacity of metastasize is a characteristic of all malignant tumors. Thus, in view of the known definition of metastasis, there is no written description for *in vivo* showing for the effectiveness of the peptides as claimed nor there is a recognized model (identified as useful) being treated according to methods of **preventing or treating a subject** for the conditions being claimed (i.e., preventing or treating primary tumor growth or metastasis).

Further, Applicant's claim is directed to prevention, and there is no objective factual evidence in the specification or references enclosed or cited by Applicant to show that prevention has occurred since no adequate time was given to mimic the protocol administered in the animal models and allow evaluation of active immune response or inhibition. Thus, one cannot administer at the point of infection and claim preventing or treating a subject for the conditions claimed without appropriate testing for the reasons of record.

6. Claims 1, 2, 6-8, 13, 14, 19, 22 and 29 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. There is no description in the instant specification for the claimed peptide comprising a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and

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contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide as claimed in independent claim 1.

Applicant has argued that endostatin is a well-known polypeptide of 184 amino acids. In addition to its biological recitation, claim 1 herein recites a peptide that comprises: a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus peptide". There are only a finite number of 7-amino acid portions of the endostatin peptide, even fewer 8-amino acid portions, and fewer yet of the larger portions up to the 20-amino acid portions. A **person skilled in the art**, upon reading the present specification, could readily envision the list of all the recited 7-20 amino acid "portions" of endostatin. That list would, of course, contain far more peptides than are covered by claim 1. A **person skilled in the art**, having read the specification, would learn what portion of the endostatin polypeptide should be obtained and would readily envision how to eliminate from the 'all 7-20 amino acid portions' list those portions that did not contain a pair of proline residues, at least one of which is at or penultimate to a terminus of the peptide "portion" of the 184 amino acid endostatin sequence. These two manipulations of the endostatin sequence, each of which is within the expected skill of the art, would leave the small group of proline-pair peptides that represent structures within claim 1 is unpersuasive.

Contrary to Applicant's arguments, the breadth of claim 1 is broad and encompasses unspecified variants regarding the length from 7-20 amino acids long and containing a pair of proline residues penultimate to a terminus of the peptide. No

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reference sequence has been provided. There is no written description indicating the claimed variants for the peptide containing a pair of proline residues at least one of which is a terminal residue penultimate to a terminus of the peptide having 7-20 amino acid length except for the elected invention of the peptide having the amino acid sequences of SEQ ID NO:30. There are no written description for other peptides comprising a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide being made or used in the instant specification.

The use of 7-20 amino acid residues with any peptide comprising a portion of an endostatin protein suggests that the amino acid sequence/residue intended to be modified by substitution is either is not known or Applicant contemplates modification of a portion of an endostatin protein by substitution from 0 to 20 of amino acid residues in the peptide. Thus, the scope of the claims is not commensurate with the written description and/or enablement provided by the disclosure with regard to the amino acid residues identified by substitution of 7-20 amino acid residues with any portion of an endostatin protein for the reasons of record.

Further, Applicant has provided a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide as disclosed in SEQ ID NO:30. From this Applicant is attempting to extrapolate to a broad diversity of a portion of an endostatin protein bearing little relationship to an

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endostatin comprising SEQ ID NO:30 disclosed in the specification by claiming the substitution of any amino acid residue having less than 20 amino acids in length. Thus, in claim 1, any number of amino acids (at least from 0 to 20) can be replaced with any number ranging from 7-20 conservative or non-conservative substitution by insertion and/or deletion. The effects of this are unknown for the reasons of record, and as such, when this variable is added, the claimed invention becomes little more than conjecture. Moreover, without guidance and/or written description, the changes which can be made in the peptide/protein structure and still maintain activity is unpredictable and the experimentation left to those skilled in the art is unnecessary and improperly, extensive and undue. See Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 927 F.2d, 1200, 18 USPQ2d 1016 (Fed. Cir. 1991) at 18 USPQ2d 1026-1027 and Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int. 1986).

Therefore, the scope of a peptide comprising a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide disclosed in the instant specification would involve substitution of the amino acid residues in the portion of an endostatin protein with any number of amino acid residues ranging from 7-20 conservative or non-conservative. Hence, it would include those that have not been shown or taught or described to be useful or enabled by the disclosed method of making and using the invention. Moreover, undue experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled, since any number of amino acid residues

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ranging from 7-20 are to be substituted with any amino acids identified as an endostatin protein are contemplated and are encompassed as well as wide range of situations.

The results desired appear to be highly dependent on all variables, the relationship of which is not clearly disclosed. Thus, without guidance and/or written description through working example(s), one of ordinary skill in the art would not predict from the sequence data disclosed in the instant specification to substitute any number of amino acid residues with a range of at least 7-20 amino acids and be used as a pharmaceutical formulation by administering a therapeutically effective amount of said pharmaceutical formulation to treat or prevent primary tumor growth or metastasis in a subject in the manner claimed in the instant invention of claims 1, 2, 6-8, 13, 14, 19, 22 and 29.

Therefore, the specification does not disclose one reasonable method of making and using the claimed invention that bears a reasonable correlation to the entire scope of the claims. The specification lacks guidance/direction and/or written description as to how employ a peptide comprising a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide in the manner as claimed in the instant invention. In summary, the scope of the claims is broad, the written description does not demonstrate the claimed variants of endostatin protein or peptide having 7-20 amino acid long, the effects of the claimed peptide is unpredictable, and the teachings or the written descriptions in the specification are limited, therefore, it is necessary to have additional guidance and/or

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written description to carry out further experimentation to assess the effects of a peptide comprising a portion of an endostatin protein, wherein said peptide is of length from 7-20 amino acids long and contains a pair of proline residues at least one of which is a terminal residue or a residue penultimate to a terminus of the peptide in the manner claimed in the instant invention of claims 1, 2, 6-8, 13, 14, 19, 22 and 29.

ACTION IS FINAL

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

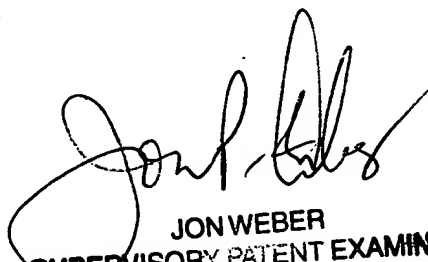
CONCLUSION AND FUTURE CORRESPONDANCE

8. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (571) 272 0955. The examiner can normally be reached on First Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, CAMPELL BRUCE can be reached on (571) 272 0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



JON WEBER
SUPERVISORY PATENT EXAMINER

Mohamed/AAM
September 15, 2005